IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Steven Z. Wu *et al.*		Examiner: Humera N. Sheikh
Serial No.	10/663,568	Art Unit: 1615
Filed:	September 15, 2003	Confirmation No.: 2840
Title:	Microparticle Coated Medical Device	

Commissioner for Patents
P.O. Box 1450
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REPLY BRIEF

Dear Honorable Board:

An Examiner's Answer was mailed July 19, 2011, in response to Applicants' Second Appeal Brief, filed March 25, 2011.

The Examiner's Answer presented new grounds of rejection, as noted at page 5 of the Examiner's Answer. Thus, the present Reply Brief addresses these new grounds of rejection. Nevertheless, any arguments not presented again from the prior appeal briefs of record should not be considered to be waived, simply because they are not explicitly repeated in this brief.

I. STATUS OF CLAIMS

Claims 25, 28-32, and 34-37 have been rejected by the Examiner; the rejections thereof are being appealed herewith. Claims 1-24, 26, 27, and 33 have been previously canceled.

II. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The grounds of rejection to be reviewed on appeal are the specific grounds of rejection exactly as set forth in the Examiner's Answer at pages 5-16 thereof. In summary, those rejections are (A) the rejection of claims 25 and 32 under 35 U.S.C. 112, first paragraph, as allegedly non-enabled (already addressed in the Second Appeal Brief filed March 25, 2011, at pp. 10-11); (B) the rejection of claims 25 and 32 under 35 U.S.C. 112, second paragraph, as allegedly indefinite (already addressed in the Second Appeal Brief filed March 25, 2011, at pp. 11-13); (C) the rejection of claims 32, 35, 36, and 37 as being obvious under 35 U.S.C. 103(a) over U.S. Patent No. 6,099,562 of Ding *et al.* ("Ding") in view of U.S. Patent Application Publication No. 2002/0133183 of Lentz *et al.* ("Lentz"); and (D) the rejection of claims 25, 28-31, and 34 as being obvious under 35 U.S.C. 103(a) over Ding in view of Lentz and further in view of U.S. Patent No. 5,886,026 of Hunter *et al.* ("Hunter").

III. ARGUMENTS

Applicants respectfully submit that, as will be explained below, each of the rejections of each of the claims is improper, and is not supported by sufficient evidence of record. Accordingly, Applicants respectfully request reversal of the rejections.

A. Claims 25 and 32 are enabled and consequently comply with 35 U.S.C. 112, first paragraph.

The errors in the rejection for alleged lack of enablement were already fully explained in Applicants' Appeal Brief. Pages 10 and 11 of the Appeal Brief provided basis for enablement of claims 25 and 32. The Examiner's response to Applicants' arguments was just to insist on an obviously wrong claim construction that requires the claim to contradict itself by both requiring and prohibiting the same thing. Such a construction of the claims cannot possibly be said to be the "broadest **reasonable** claim construction," and consequently is plainly improper.

Claim 25 recites, "a coating layer disposed on the stent body, and polymeric particles containing a therapeutic substance embedded within the coating layer, wherein the coating layer comprises a polymer different than the polymer from which the particles are made, wherein the coating layer is free from any therapeutic substances." Properly understood this claim requires three things: a coating layer, polymeric particles embedded within the layer (but not treated as part of the coating layer for the purposes of the claim), and therapeutic substance only in the polymeric particles, but not in the coating layer (not considering the polymeric particles). An example of this can be seen in Figure 2. In Figure 2, coating layer 18 has embedded microparticles 20. The microparticles can be "drug-loaded" as explained at page 7, line 9, of the application as filed. Under that proper understanding of the claims, there is no self-contradiction. However, under the claim construction advocated in the Examiner's Answer "coating layer" refers both to the layer itself and to the polymer particles embedded within the layer. This leads to a self-contradiction, since the particles must contain therapeutic substances, whereas the coating

layer does not. Therefore, the claim construction in the Examiner's Answer is unreasonable.

Additionally, under the claim construction advocated in this section of the Examiner's Answer, the rejections for alleged obviousness could not be maintained, since the prior art cannot possibly meet the limitations construed to be self-contradictory. Of course, this highly unreasonable claim construction was not used in rejecting the claims on the basis of the prior art. Such a claim construction should not have been used in this rejection either.

To reiterate, claim 25's recitation, "polymeric particles containing a therapeutic substance embedded within the coating layer, ... wherein the coating layer is free from any therapeutic substances" distinguishes an embodiment in which the coating layer itself contains therapeutic substances, as opposed to an embodiment in which only the polymeric particles contain a therapeutic substance. This is a reasonable claim construction that avoids the self-contradiction inherent in the claim construction argued in the Examiner's Answer.

Claim 32 is also enabled in light of the specification. Claims 32 recites "wherein the coating layer is free from any therapeutic substances **but** includes particles of a polymeric material having a therapeutic substance added thereto, wherein the therapeutic substance is completely encased within the polymer particles." As outlined on pages 10 and 11 of the Appeal Brief, Examples 1-8 and Method 1 (as well as Methods 2 to 6) of the specification enable the claimed coating construct.

B. Claims 25 and 32 are definite and consequently with 35 U.S.C. 112, second paragraph.

The rejection for alleged lack of definiteness has the same self-contradictory claim construction as the previous claim construction, and was also already fully addressed in the Appeal Brief. Applicants respectfully submit that the allegedly "confusing and unclear" terminology is not **reasonably** susceptible to another meaning than the meaning already explained by Applicants. While the Examiner has refused to accept this meaning and instead imposes a self-contradictory meaning on the claims for the purpose of rejecting the claims under this section (though not under other sections

involving prior art), the claims read in light of the specification are definite and unambiguous.

Indeed, when the only other meaning (besides Applicants' proposed meaning) is a self-contradiction, it is correct to say that the claims are plainly unambiguous. Thus, the claims not indefinite in any way.

In summary, in light of the specification it is abundantly clear that "free from any therapeutic substances" refers to the coating itself (reference number 18 of Figure 2), which is formed from a solution without any dissolved therapeutic substances. In contrast, the microparticles -- containing or encasing the therapeutic substances -- are suspended in this solution, but do not dissolve in the solution. Thus, therapeutic substances can be held on the stent by the layer 18, but are not part of the layer 18 from the standpoint of the claim. The cited portions of the specification provide the light necessary so that the metes and bounds of the invention can be clearly understood without self-contradiction, as more fully explained in Applicants' Second Appeal Brief.

In finding Applicants' arguments for both the 112 first paragraph and second paragraph rejections of claims 25 and 32 unpersuasive, the Examiner reasoned that "even though the polymeric particles encasing the therapeutic agent is suspended within the coating, as opposed to dissolved in the coating, the coating layer still contains a therapeutic substance. A suspension is defined as a mixture in which small particles of a substance are dispersed throughout a liquid. This differs from a solution where a particle would dissolve in a solvent and no longer maintain the particulate form." (emphasis added). The Examiner concluded that "particles suspended in a coating are still incorporated in the coating layer." (see page 17 for 112, first paragraph response and page 18 for 112, second paragraph response.)(emphasis added)

Claims 25 and 32 do not recite a "suspension." Claims 25 and 32 do not provide "particles suspended in a coating" as asserted by the Examiner. The term "suspended" appears only in claim 36, which is directed to a process of making a coating construct having the polymeric particles. Accordingly, the definition of suspension is completely irrelevant in constructing claims 25 and 32, and maintaining a rejection based on this definition is unfounded. The Examiner's rebuttal appears to be based on Applicants' description on how to make the coating construct of the present invention. In the Appeal

Brief, the Applicants noted that the specification provides a method of applying a polymer solution which includes a suspension of the agent-loaded microparticles to the medical device. The suspension of the particles in a polymer solution was provided in support of showing enablement of the invention and not for the term to be incorporated into the claims.

C. Claims 32 and 35-37 are non-obvious with respect to U.S. Patent No. 6,099,562 of Ding *et al.* ("Ding") in view of U.S. Patent Application Publication No. 2002/0133183 of Lentz *et al.* ("Lentz")

Prior to addressing the merits of this new rejection, Applicants would like to respectfully address the grounds for this rejection. The Examiner has now removed the anticipatory 102(e) rejection under Ding and contends that claims 32 and 35 -37 are obvious over Ding and Lentz. The Examiner has noted on page 5 of the Examiner's Answer that the rejection "brings the claims... under the previously-made rejection of the other claims under 35 USC 103." More particularly, the Examiner has contended that "this new ground of rejection is not seen to create issues not already presented in the application but merely corrects the oversight of not including all claims in the rejections under 35 USC 103." (emphasis added).

Applicants respectfully disagree. The foundation of the rejection has changed. The Examiner has now created issues which were not previously presented. The Examiner's previous position was that Ding taught therapeutic substances encased within polymeric particles (see, for example, pages 4 and 7 of the Office Action dated May 25, 2010). In fact on page 11 of the Examiner's Answer, lines 16-19, with respect to claims 25, 28-31 and 34, the Examiner reiterated the previous position that Ding teaches therapeutic substances encased within polymeric particles. However, in providing a new ground of rejection for claims 32 and 35-37, on page 7 of the Examiner's Answer, the Examiner has noted, "Ding does not teach a therapeutic substance encased within polymeric particles." This statement is certainly contrary to the Examiner's initial position in the Office Action and more significantly cannot even be reconciled with the Examiner statement made with reference to claims 25, 28-31, and 34.

The Examiner's new position is that Lentz teaches polymeric particles encasing a therapeutic substance. It also appears that the Examiner is contending that Lentz teaches the remaining elements of the claim, including the coating layer having a polymer different than the polymer from which the particles are made and that the coating layer is free from any therapeutic substances. Based on the Examiner's analysis on pages 6-9, it appears that Berg is completely irrelevant to the new rejection that is being provided. Under the Examiner's analysis, Berg's teachings appear to be moot, yet Berg is still being cited for reasons that are not well explained.

Since the Applicants are on the second appeal, Applicants prefer to maintain this appeal and forgo reopening of the prosecution.

1. Claim 32 is Non-Obvious With Respect to the Combination of Ding and Lentz

The Examiner's Answer, at page 6, noted that Ding teaches that "[t]he coating is preferably applied as a mixture, solution, or suspension of polymeric materials and finely divided biologically active species dispersed in an organic vehicle or a solution or partial solution of such species in a solvent or vehicle for the polymer and/or biologically active species (col. 4, lines 8-13)." However, the Examiner's Answer, at page 7, admitted that "Ding does not teach a therapeutic substance encased within polymeric particles." The Examiner's Answer cited Lentz to remedy such deficiencies of Ding.

Lentz states in paragraph [0088], cited in the Examiner's Answer:

> The best conditions for the coating application are when the polyfluoro copolymer and pharmaceutic agent have a common solvent. This provides a wet coating that is a true solution. Less desirable, yet still usable, are coatings that contain the pharmaceutical agent as a solid dispersion in a solution of the polymer in solvent. ... In cases where a dispersion is applied to the stent and the smoothness of the coating film surface requires improvement, or to be ensured that all particles of the drug are fully encapsulated in the polymer, or in cases where the release rate of the drug is to be slowed, a clear (polyfluoro copolymer only) topcoat of the same polyfluoro copolymer used to provide sustained release of the drug or another polyfluoro copolymer that further restricts the diffusion of the drug out of the coating may be applied.

The Examiner's Answer alleged that this disclosure teaches "whereby particles of drug are fully encapsulated in the polymer." However, Applicants respectfully submit that there is no disclosure of "particles of a polymeric material having a therapeutic substance added thereto, wherein the therapeutic substance is completely encased within the polymer particles," as recited in claim 32, whether or not particles of a drug are disclosed as encapsulated in the polymer. Therefore, Lentz does not remedy the above-identified and admitted (by the Examiner) deficiencies of Ding.

Additionally, while Lentz mentions the option of a dispersion, Lentz explicitly indicates that such an approach is "less desirable," thereby teaching away from such an approach. Accordingly, even if the dispersion approach of Lentz could somehow be viewed as relevant to the claim recitations, Lentz teaches away from this approach.

Additionally, there is no explanation at all in the Examiner's Answer as to what would have led one ordinary skill in the art to have modified Ding with such a feature of Lentz. Accordingly, the rejection cannot be maintained, because the rejection cannot meet the standard for obviousness set forth in *KSR* and the other precedent identified above.

The Examiner's Answer, at page 8, asserted: "Therefore, even though several layers are applied, the act of cross-linking these layers creates one layer, wherein other polymers are present that are different from the polymer particles encapsulating the therapeutic agent." However, it is respectfully submitted that Lentz does not mention polymer particles encapsulating a therapeutic agent. Accordingly, whether or not cross-linking operates as alleged, this assertion does not appear to be pertinent to the disclosure of Lentz.

The Examiner's Answer further erroneously asserts that the expression "all particles of the drug are fully encapsulated in **the** polymer" (emphasis added in Examiner's Answer) implies that only a single polymer necessarily encapsulates the drug in Lentz. That same sentence (see paragraph [0088] of Lentz) which states "encapsulated in the polymer" explains that full encapsulation can be achieved by a "topcoat of the same polyfluoro copolymer ... or another polyfluoro copolymer ... ." Therefore, the Examiner's Answer has improperly emphasized the definite article in Lentz. Moreover, as explained above, whether or not Lentz discloses enclosing particles of drug in polymer,

Lentz does not disclose "particles of a polymeric material having a therapeutic substance added thereto, wherein the therapeutic substance is completely encased within the polymer particles," as recited in claim 32.

2. Claim 35 is Non-Obvious With Respect to the Combination of Ding and Lentz

Claim 35 recites "wherein the coating layer comprises a polymer different than the polymer from which the particles are made." The Examiner's Answer acknowledged that Ding does not disclose these features. The Examiner's Answer cited Lentz to remedy these deficiencies.

However, Lentz's particles are "particles of the drug." There is no indication in Lentz that the particles are particles of a polymer. Therefore, whether or not Lentz suggests using multiple polymers in general, Lentz does not remedy Ding's deficiencies with respect to the feature of claim 35.

It is not clear in the Examiner's Answer where the detailed explanation of the rejection of claim 35 is to be found. Nevertheless, as best understood, the Examiner took the position that these features are disclosed by Lentz, because Lentz teaches "wherein different polyfluoro copolymers may be used for different layers in the stent coating." (emphasis omitted) However, different layers of the stent coating cannot correspond to "wherein the coating layer comprises a polymer different than the polymer from which the particles are made," as recited in claim 35, because there is a difference between a "layer" and a "particle."

3. Claim 36 is Non-Obvious With Respect to the Combination of Ding and Lentz

Claim 36 recites, "adding polymeric particles containing a therapeutic substance to a fluid form of an implantable medical device coating material." There is no disclosure of these features in Ding. The Examiner's Answer took the position that these are product-by-process limitations. The Examiner's Answer specifically argued:

> With respect to claims 36 and 37, which recite product-by-process limitations, the Examiner notes "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the

> product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

Even assuming this accurately represents part of the law regarding product-by-process limitations, the Examiner is still required to show that the products of the prior art are equivalent to products formed according to the claim. Specifically, as stated in MPEP 2113:

> The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979) (holding "interbonded by interfusion" to limit structure of the claimed composite and noting that terms such as "welded," "intermixed," "ground in place," "press fitted," and "etched" are capable of construction as structural limitations.)

However, the structure that results from the process of "adding polymeric particles containing a therapeutic substance to a fluid form of an implantable medical device coating material, wherein the coating material includes a polymeric material dissolved in a solvent, and wherein the polymeric particles containing the therapeutic substance are suspended in the polymeric material dissolved in the solvent," is not found in the prior art and is not obvious in view of the prior art.

The Examiner's Answer alleged "It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate different polymeric coatings onto an implantable device, such as a stent, as taught by Lentz, within the devices of Ding." However, such a combination does not result in a structure similar to the structure produced by the method of claim 36. Claim 36 does not merely mention "different polymeric coatings," but instead describes "polymeric particles containing a therapeutic substance" that are added to a fluid form including a polymeric material dissolved in a solvent.

The Examiner's Answer also alleged "Lentz explicitly teaches implantable medical devices (i.e., stents) provided with polymeric coatings (i.e., polyfluoro copolymers) to deliver pharmaceutically active material, whereby particles of drug are fully encapsulated in the polymer, and other polymers, different from the polyfluoro polymer, may be added to the coating composition." However, what the claim recites is not simply that the particles of drug are fully encapsulated by polymer, but that polymer particles contain a therapeutic substance and then these polymeric particles exist as a suspension in a fluid form of polymeric material dissolved in solvent. There are no corresponding "polymeric particles containing a therapeutic substance" in either Ding or Lentz.

On page 9 of the Examiner's Answer, the Examiner stated, "by encapsulating a therapeutic particle with a polymer, the polymer in turn becomes a particle." (emphasis added) Applicants respectfully submit that this statement is not only specious but grossly incongruous. All that Lentz teaches is that (1) the solvent can be mutual to both the polymer and the drug so that a true solution is formed or (2) the solvent is just for the polymer and not the drug such that the drug will present itself in particles once the solvent is evaporated. Presentation of the drugs in particles in a polymer does not inexplicably change the polymer into particles encasing the drug as contended by the Examiner, more so since the polymer is taught to be dissolved in the solvent. Once the solvent is evaporated, what remains is a polymer coating layer having particles of the drug embedded within the coating layer. Therefore, the structure implied by the process steps of the product-by-process claims is not found in or obvious in view of the prior art. Therefore, the rejection of claim 36 must be reversed.

4. Claim 37 is Non-Obvious With Respect to the Combination of Ding and Lentz

Claim 37 depends from claim 36. Thus, the rejection of claim 37 should be reversed for at least the same reasons that the rejection of claim 36 should be reversed. Claim 37 further recites: "wherein the film layer includes the polymeric material encasing the polymeric particles." There is no discussion in Ding or Lentz of any polymeric material encasing polymeric particles. Accordingly, the combination of Ding and Lentz does not disclose or suggest at least these further features of claim 37. Thus, for this

additional and alternative reason, it is respectfully requested that the rejection of claim 37 be reversed.

D. Claims 25, 28-31, and 34 are non-obvious with respect to Patent No. 6,099,562 of Ding *et al.* ("Ding") in view of U.S. Patent Application Publication No. 2002/0133183 of Lentz *et al.* ("Lentz") and further in view of U.S. Patent No. 5,886,026 of Hunter *et al.* ("Hunter").

"[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." (*KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 418, (2007) It is respectfully submitted that, for the reasons set forth below, the rejections of the claims do not meet the standard required for a *prima facie* rejection for non-obviousness.

1. Claim 25 is Non-Obvious With Respect to the Combination of Ding, Lentz, and Hunter

Claim 25 recites, "polymeric particles containing a therapeutic substance embedded within the coating layer" and "wherein the coating layer is free from any therapeutic substances." As discussed above, with respect to claim 32, the combination of Ding and Lentz does not disclose these features. Hunter cannot remedy these deficiencies of Ding and Lentz, which is not surprising, because it was not cited with respect to such features. Thus, for at least these independent and alternative reasons, the rejection of claim 25 should be reversed.

In this rejection, the Examiner's Answer argued (page 11):

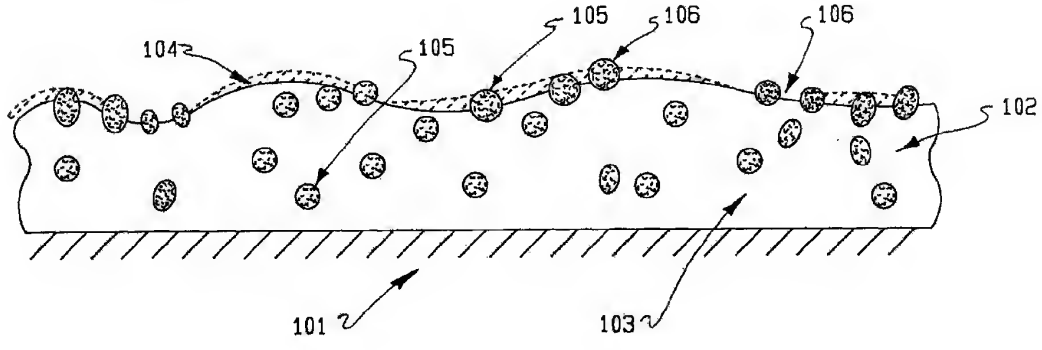
> The coating [of Ding] is preferably applied as a mixture, solution or suspension of polymeric material and finely divided biologically active species dispersed in an organic vehicle or solution or partial solution of such species in a solvent or vehicle for the polymer and/or biologically active species (col. 4, lines 8-13). This reads on Applicant's medical device having a 'coating layer wherein the therapeutic substance completely encased within polymer particles' and 'film layer including polymeric material encasing the polymeric particles'. The term "finely

> divided" refers to any type or size of included material from dissolved molecules through suspensions, colloids and particulate mixtures. The active material is dispersed in a carrier material which may be the polymer, a solvent or both. The coating is preferably applied as a plurality of relatively thin layers sequentially applied in relatively rapid sequence and is preferably applied with the stent in a radially expanded state (col. 4, lines 14-21).

(emphasis added)

First, the Examiner's position is entirely inconsistent with the position presented with respect to claims 32 and 35-37. For claims 32 and 35-37, the Examiner unequivocally stated that "Ding does not teach a therapeutic substance encased within polymeric particles." (page 7, line 20, Examiner's Answer). Now the Examiner is contending the opposite, that Ding teaches "a coating layer wherein the therapeutic substance [is] completely encased within polymer particles." Both positions simply cannot be reconciled.

Second, Ding does not disclose therapeutic substance being completely encased within polymer particles. Example 1 of the present application, at page 8 provides a non-limiting example of how microparticles containing a therapeutic substance can be created. There is nothing similar in Ding. Instead, Ding merely describes incorporating therapeutic particles into a polymeric layer. Specifically, refer to the cover illustration of Ding (Figure 9), duplicated below:



Items 105 of Ding are "drug particles 105." There is nothing in Ding that suggests that these are polymeric particles including, containing, or completely encasing a drug. Instead, they are simply particles of the drug itself.

Claim 25 also recites, "wherein the coating layer comprises a polymer different than the polymer from which the particles are made." The Examiner's Answer admitted that Ding fails to disclose "wherein the coating layer comprises a polymer different than the polymer from which the particles are made." The Examiner's Answer cited Lentz with respect to this feature. However, according to the Examiner's characterization (page 13 of the Examiner's Answer), Lentz discloses "different polyfluoro copolymers may be used for different layers in the stent coating." However, such a disclosure is not equivalent to "wherein the coating layer comprises a polymer different than the polymer from which the particles are made." After all, the alleged disclosure of Lentz relates to *different layers* not to particles embedded within a layer.

Indeed, the Examiner's rationale for the alleged motivation to combine Ding and Lentz is directed to use multiple polymeric coatings. Such features would not lead to the features recited in claim 25. Thus, Lentz would not lead one of ordinary skill in the art to modify Ding to arrive at the invention recited in claim 25, because it could not cure even the deficiencies of Ding acknowledged in the Examiner's Answer with respect to claim 25.

The teachings of Hunter were not applied to claim 25, and it is respectfully submitted that no teachings of Hunter would lead one of ordinary skill in the art to modify Ding so as to arrive at the invention recited in claim 25. Thus, for all or any of these reasons, it is respectfully requested that the rejection of claim 25 be reversed.

At page 22, in the "Response to Arguments" section, the Examiner's Answer argued that "A therapeutic particle completely encapsulated by a polymer would in turn result in a polymeric particle." This is not true. Not every therapeutic particle completely encapsulated by a polymer is in the form of a polymeric particle. In some cases, a therapeutic particle completely encapsulated by a polymer is a polymeric layer. Indeed, that is all that the prior art discloses: polymeric layers with therapeutic materials therein. There is no disclosure of polymeric particles that contain therapeutic materials.

It appears that the Examiner's Answer has not properly construed "polymeric particle" to be a particle such as, for non-limiting example, a microparticle described in Example 1 of the present application. Instead, the Examiner's Answer has improperly construed "polymeric particle" to refer to a layer that includes drug particles. This

improper claim construction can and should serve as a basis upon which the rejection of claim 25 is reversed.

2. Claim 28 is Non-Obvious With Respect to the Combination of Ding, Lentz, and Hunter

Claim 28 depends from, and further limits, claim 25. Thus, for at least any or all of the reasons that the rejection of claim 25 should be reversed, the rejection of claim 28 should also be reversed.

Claim 28 further recites, "wherein the polymeric particles are made from a hydrogel material." The only mention in Ding of "hydrogel" is in the "related art" section. That section refers to using "a coating applied to a stent consisting of a hydrogel polymer and a preselected drug such as cell growth inhibitors or heparin." However, there is no disclosure that such a hydrogel polymer could or should be made into polymeric particles.

Likewise, there is no mention of "hydrogel" in Lentz, whereas in Hunter, hydrogel compositions are discussed as follows: "Stents may be coated with anti-angiogenic compositions or anti-angiogenic factors of the present invention in a variety of manners, including for example: ... by coating the stent with a substance such as a hydrogel which will in turn absorb the anti-angiogenic composition (or anti-angiogenic factor above) ... ."

The Examiner's Answer does not make clear what part of the prior art is relied upon as allegedly teaching "wherein the polymeric particles are made from a hydrogel material." Thus, no *prima facie* rejection of claim 28 has been made. Nevertheless, based on a review of all the prior art of record, it is respectfully submitted that the prior art of record does not disclose or suggest "wherein the polymeric particles are made from a hydrogel material," as recited in claim 28. Thus, for this additional and alternative reason, it is respectfully requested that the rejection of claim 28 be reversed.

3. Claim 29 is Non-Obvious With Respect to the Combination of Ding, Lentz, and Hunter

Claim 29 depends from, and further limits, claim 25. Thus, for at least any or all

of the reasons that the rejection of claim 25 should be reversed, the rejection of claim 29 should also be reversed. Claim 29 is being argued separately to preserve Applicants' right to have claim 29 separately considered as patentable in case the grounds of rejection change yet again.

4. Claim 30 is Non-Obvious With Respect to the Combination of Ding, Lentz, and Hunter

Claim 30 depends from claim 25. Thus, for at least any or all of the reasons that the rejection of claim 25 should be reversed, the rejection of claim 30 should also be reversed. Claim 30 is being argued separately to preserve Applicants' right to have claim 30 separately considered as patentable in case the grounds of rejection change yet again.

5. Claim 31 is Non-Obvious With Respect to the Combination of Ding, Lentz, and Hunter

Claim 31 depends from claim 25. Thus, for at least any or all of the reasons that the rejection of claim 25 should be reversed, the rejection of claim 31 should also be reversed. Claim 31 is being argued separately to preserve Applicants' right to have claim 31 separately considered as patentable in case the grounds of rejection change yet again.

6. Claim 34 is Non-Obvious With Respect to the Combination of Ding, Lentz, and Hunter

Claim 34 depends from claim 25. Thus, for at least any or all of the reasons that the rejection of claim 25 should be reversed, the rejection of claim 34 should also be reversed.

Additionally, claim 34 recites, "wherein the therapeutic substance is completely encased within the polymeric particles." However, the combination of Ding, Lentz, and Hunter does not disclose or suggest even having particles that contain a therapeutic substance, much less particles that completely encase the therapeutic substance, as already discussed above. The arguments in the Examiner's Answer with respect to these features have already been addressed, therefore, based on the failure of the prior art to show "polymeric particles containing a therapeutic substance embedded within the

coating layer." Accordingly, it is respectfully requested that the rejection of claim 34 be reversed.

IV. CONCLUSION

For all of the foregoing reasons it is submitted that all of the Examiner's rejections of claims 25, 28-32, and 34-37 were in error, and reversal of the Examiner's rejections and allowance of the application are respectfully requested.

The Commissioner is hereby authorized to charge Deposit Account No. 07-1850 for any fees due.

Respectfully submitted,

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Enclosure: Claims Appendix (for the Honorable Board's convenience)

Claims Appendix

25. A drug loaded stent, comprising:

a radially expandable stent body,

a coating layer disposed on the stent body, and

polymeric particles containing a therapeutic substance embedded within the coating layer, wherein the coating layer comprises a polymer different than the polymer from which the particles are made, wherein the coating layer is free from any therapeutic substances.

28. The stent of Claim 25, wherein the polymeric particles are made from a hydrogel material.

29. The stent of Claim 25, wherein the particles are 0.5 to 2 microns in size.

30. The stent of Claim 25, wherein the therapeutic substance is for the treatment of restenosis.

31. The stent of Claim 25, wherein the therapeutic substance is a radioactive isotope.

32. A medical device, comprising an implantable substrate and a coating layer, wherein the coating layer is free from any therapeutic substances but includes particles of

a polymeric material having a therapeutic substance added thereto, wherein the therapeutic substance is completely encased within the polymer particles.

34. The stent of claim 25, wherein the therapeutic substance is completely encased within the polymeric particles.

35. The medical device of claim 32, wherein the coating layer comprises a polymer different than the polymer from which the particles are made.

36. An implantable medical device made by the method comprising:

adding polymeric particles containing a therapeutic substance to a fluid form of an implantable medical device coating material, wherein the coating material includes a polymeric material dissolved in a solvent, and wherein the polymeric particles containing the therapeutic substance are suspended in the polymeric material dissolved in the solvent;

applying the fluid form of the coating material comprising the polymeric particles added thereto to an implantable medical device; and

solidifying the coating material to a film layer by allowing the solvent to evaporate, wherein the film layer includes the polymeric particles containing the therapeutic substance.

37. The implantable medical device of claim 36, wherein the film layer includes the polymeric material encasing the polymeric particles.